



National Arthritis and  
Musculoskeletal and  
Skin Diseases Advisory Council

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# **MINUTES OF MEETING**

**February 27, 2007**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
NATIONAL ARTHRITIS AND MUSCULOSKELETAL  
AND SKIN DISEASES ADVISORY COUNCIL**

**MINUTES OF THE 61st MEETING**

**February 27, 2007  
8:30 a.m. to 4:00 p.m.**

**I. CALL TO ORDER**

The 61st meeting of the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council was held on February 27, 2007, at the National Institutes of Health (NIH) Campus, Building 31, Conference Room 6. The meeting was chaired by Dr. Stephen Katz, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

**Attendance**

Council members present:

Mr. George A. Beach  
Dr. Gena R. Carter  
Ms. Carmen Cheveres DeMummey  
Dr. Betty Diamond  
Dr. Kathleen Green  
Dr. Bevra H. Hahn  
Dr. Joshua Jacobs  
Dr. Brian L. Kotzin  
Dr. Martin J. Kushmerick  
Ms. Patricia McCabe (by telephone)  
Dr. Jack E. Parr  
Dr. Lawrence G. Raisz (by telephone)  
Dr. Clifford J. Rosen  
Dr. Raymond Scalettar  
Dr. Jouni J. Uitto  
Dr. James Weinstein

Council members not present:

Dr. Kevin Campbell  
Dr. Lee Green  
Dr. Robert J. Oglesby (Ex Officio)

## **Staff and Guests:**

The following NIAMS staff and guests attended:

### Staff

Dr. Janet Austin  
Dr. Carl Baker  
Dr. Susan Bettendorf  
Dr. Michael Bloom  
Mr. Gahan Breithaupt  
Dr. Eric Brown  
Mr. Richard Clark  
Mr. Frank Cromwell  
Ms. Teresa Do  
Ms. Jonelle Drugan  
Mr. Patrick Durand  
Mr. Erik Edgerton  
Ms. Sharon Fair  
Dr. Elizabeth Gretz  
Ms. Gail Hamilton  
Mr. Saji Ijiyemi  
Dr. Stephen Katz  
Ms. Shahnaz Khan  
Mr. Mark Langer  
Dr. Cheryl Lapham  
Dr. Gayle Lester  
Dr. Helen Lin  
Ms. Anita Linde  
Ms. Elizabeth Lordan  
Dr. Kan Ma  
Dr. Marie Mancini  
Dr. Joan McGowan  
Ms. Leslie McIntire  
Dr. Glen Nuckolls  
Dr. John O'Shea  
Dr. Jim Panagis  
Ms. Wilma Peterman  
Dr. Paul Plotz  
Ms. Trish Reynolds  
Dr. Louise Rosenbaum  
Dr. Susana Serrate-Sztejn  
Dr. Bill Sharrock  
Ms. Theresa Smith  
Ms. Robyn Strachan  
Mr. Yen Thach

Mr. Michael Toland  
Dr. Madeline Turkeltaub  
Dr. Bernadette Tyree  
Dr. Fei Wang  
Dr. Ping Wang  
Dr. Yan Wang  
Dr. Chuck Washabaugh  
Dr. James Witter

### Guests

Dr. Barbara Alving, National Center for Research Resources, NIH  
Mr. John Bartram, Office of the Director, NIH  
Ms. Patti Brandt-Hansberger, Office of Legislative Policy and Analysis, NIH  
Ms. Jodie Curtis, National Psoriasis Foundation  
Ms. Ann Elderkin, American Society for Bone and Mineral Research  
Ms. Christy Gilmour, American Academy of Orthopaedic Surgeons  
Ms. Darlene Kerr, Circle Solutions  
Dr. Cheryl Kitt, Center for Scientific Review, NIH  
Ms. Sheila Rittenberg, National Psoriasis Foundation  
Dr. Tony Scarpa, Center for Scientific Review, NIH  
Mr. Marc Smolonsky, Office of the Director, NIH  
Mr. David Vovakes, Office of the Director, NIH  
Ms. Roxanne Yaghubi, Society of Investigative Dermatology

## II. CONSIDERATION OF MINUTES

A motion was made, seconded, and passed to accept the minutes of the 60<sup>th</sup> Council meeting, held on September 26, 2006.

## III. FUTURE COUNCIL DATES

Future Council meetings are currently planned for the following dates:

June 12, 2007  
September 27, 2007  
January 29, 2008  
June 6, 2008  
September 23, 2008  
February 3, 2009  
June 2, 2009  
September 16, 2009

Dr. Katz informed Council members that the Council meeting originally scheduled for May 27, 2008 will be held on June 6, 2008. The date was changed because of its proximity to Memorial

Day Weekend. He asked Council members to ensure that their calendars were updated with this change.

#### IV. DIRECTOR'S REPORT AND DISCUSSION

Dr. Katz began his report by inviting Council members to review the NIAMS Shorttakes online, which go into more detail on many of the topics covered in this Director's Report.

##### **New Council Members**

Dr. Katz introduced the following new Council members:

- **George A. Beach**, Chairman and CEO of Beach Communications. Mr. Beach is a patient with rheumatoid arthritis who has been an active member of the Arthritis Foundation for many years as well as many other organizations, such as the Alliance for Aging.
- **Dr. Betty Diamond**, Chief of the Laboratory of Autoimmune Diseases at the Feinstein Institute of Medical Research/North Shore Health System and Professor at the Albert Einstein College of Medicine. Dr. Diamond is starting a center for lupus research at North Shore and is developing additional centers for lupus research throughout New York. She also is slated to serve as President of the Association of American Immunologists.
- **Dr. Kathy Green**, the Joseph L. Mayberry Professor in the Department of Pathology at Northwestern University Medical School and Professor of Dermatology and Associate Chair for Research and Graduate Education in Pathology at Northwestern. Dr. Green's research has been focused on cell and skin biology.
- **Dr. Clifford Rosen**, Professor of Nutrition at the University of Maine and Executive Director of the Maine Center for Osteoporosis Research and Education. Dr. Rosen has served as President of the American Society for Bone Mineral Research, and has been very active in the bone and endocrinology fields.
- **Dr. James Weinstein**, Professor and Chair of the Department of Orthopaedics at Dartmouth-Hitchcock Medical Center. Dr. Weinstein also is the Director of the Institute for Informed Patient Choice at Dartmouth University Medical School, and his focus has been on orthopaedic surgery and health outcomes research.

Dr. Katz commented that all of these new Council members bring scientific expertise and a demonstrated commitment to scientific excellence and improved public health.

##### **Personnel Changes at the NIH and NIAMS**

NIH Director Dr. Elias Zerhouni has announced that Dr. Alan M. Krensky has been named as the first NIH Deputy Director for the Office of Portfolio Analysis and Strategic Initiatives (OPASI).

In terms of NIAMS staff, Dr. Steven Hausman has retired after more than 20 years of service to the NIAMS, during which he served as the Institute's first and only Deputy Director to date. A search for the new Deputy Director is underway. Dr. Paul Plotz, Chief of the Arthritis and Rheumatism Branch in the NIAMS Intramural Research Program, has agreed to serve as the Acting Deputy Director. In the NIAMS Intramural Research Program, Dr. Mark Gourley has accepted the position of Director of the Rheumatology Fellowship Training Program. Dr. Gourley was most recently a staff clinician at the National Institute of Environmental Health Sciences, working on environmental causes of lupus and other autoimmune diseases.

In the Extramural Research Program, Dr. Cheryl Lapham recently joined the Institute as a Program Director in the Skin and Rheumatic Diseases Branch. Since 2002, she has served as a Scientific Review Administrator (SRA) in the AIDS Preclinical Review Branch and as Acting Chief of the Immunology Preclinical Review Branch in the Scientific Review Program at the National Institute of Allergy and Infectious Diseases. Dr. Marie Mancini recently joined the Extramural Program as a Program Director in the Skin and Rheumatic Diseases Branch. Previously, she was a Research Scientist at MedImmune, and has worked in the Surgery Branch at the National Cancer Institute. Dr. James Witter currently is on detail to the NIAMS from the U.S. Food and Drug Administration, where he served as Medical Officer Team Leader in the Center for Drug Evaluation and Research since 1995. Teresa Smith has joined the NIAMS as a Research Program Analyst in the Musculoskeletal Diseases Branch; she came to the NIH 3 years ago as a biomedical engineer in the National Institute for Biomedical Imaging and Bioengineering (NIBIB). Elijah Weisberg, a Research Program Analyst in the Musculoskeletal Diseases Branch, also came to the NIAMS from the NIBIB. Before joining NIAMS, he worked at Yale New Haven Hospital as a clinical researcher. Shahnaz Khan has joined the Institute as a Clinical Coordinator in the Extramural Program. She graduated from George Washington University and is working on her Masters degree in Public Health with a concentration in epidemiology.

Wilma Peterman Cross has joined the NIAMS Office of Science Policy and Planning, handling the responsibilities of the Office's Deputy Director. Dr. Jonelle Drugan has joined the NIAMS Office of Science Policy and Planning (OSPP) as a Science Policy Analyst after working at the National Heart, Lung and Blood Institute. Dr. Louise Rosenbaum also has joined the NIAMS OSPP as a Policy Analyst. Previously, she worked in the Office of Sponsored Projects at Dartmouth College. Trish Reynolds, a Registered Nurse, has joined the NIAMS Office of Communications and Public Liaison as a Writer/Editor.

### **Update on Congressional Activity**

The NIH Reform Act of 2006 was signed by the President on January 15, 2007; this Act represents a significant endorsement of biomedical research and NIH's role in supporting it. The Act includes a number of provisions, and the NIH is now in the process of developing plans to implement them. One provision establishes the Division of Program Coordination Planning and Strategic Initiatives (currently known as OPASI).

## Highlights of Recent Scientific Advances

- Studies by Drs. Richard Eckerts and Kathleen Lee reported in the *Journal of Investigative Dermatology* identify a new type of defensin: psoriasin, a protein markedly increased in epidermal hyperproliferative disorders. This protein, like other defensins, is now shown to be highly expressed in human wound tissue and to have antibacterial effects.
- A study published in the *American Journal of Human Genetics* by Dr. Angela Christiano and colleagues described a genome-wide scan for linkage that revealed evidence of several susceptibility loci for alopecia areata on chromosomes 6, 10, 16, and 18. This work represents an investment the Institute made in developing a registry and repository for alopecia areata; these results are the first to come from this investment, which started 4-5 years ago. More information in terms of localization of these susceptibility loci is expected in the future.
- A paper in *Arthritis and Rheumatism* by Dr. Benoit de Crombrugge and colleagues describes the development of a mouse model of systemic sclerosis. The model was established to assess the effect of transforming growth factor (TGF)  $\beta$  signaling pathways in systemic sclerosis. The researchers found that it was a constantly activated pathway, causing a phenotype characteristic of systemic sclerosis; a disease in dire need of new pathway discovery. The TGF  $\beta$  pathway appears to be a promising one.
- Dr. Michael Brenner and coworkers published a paper in *Science Express* on the importance of cadherin-11 in synovial lining formation and pathology in arthritis. A mouse model was used to show that the synovial cadherin-11 is essential for the development of the synovium, and the protein determines the behavior of synovial cells and their proinflammatory and destructive tissue response in inflammatory arthritis. Cadherin-11 deficient mice were found to be resistant to inflammatory arthritis.
- Angiotensin II type I receptor blockade has been found to attenuate TGF  $\beta$ -induced failure of muscle regeneration in multiple myopathic states. Studies from Dr. Harry (Hal) Dietz and colleagues published in *Science* 4-5 months ago reported that in a Marfan syndrome mouse model, early treatment of the angiotensin II type I receptor blockade with Losartin, a commonly used drug, blocked the development of Marfan syndrome in these experimental mice at 5-7 days treatment postnatal life. This group also reported in *Nature Medicine* on the effects of Losartin in states where fibrosis is an issue. For example, in Duchenne Muscular Dystrophy, this group found that Losartin was effective in blocking the key mechanism of the fibrosis associated with this disorder. Not only did the investigators demonstrate that it was beneficial morphologically, they also showed that it was functionally beneficial. Other groups are trying to replicate this work.
- A paper by Dr. Jim Weinstein, a member of the Advisory Council, and colleagues published in the *Journal of the American Medical Association* described the outcomes of surgical versus non-operative approaches to treating lumbar disk herniation. The NIAMS has made a long-term investment in this area to better identify the differences between surgical and non-surgical treatment of lower back pain. This 13-center study demonstrated that doctors and

patients have reasons to reconsider surgery when planning treatment for herniated disks. In this study of candidates for lumbar discectomy, they found that those who elected for non-operative care in lieu of surgery fared similarly to those who had the surgery. In general, however, those who had the surgery experienced slightly more improvement over the study period, particularly over the first 3 months than those who opted for other treatments.

- NIAMS's long-term investment in the study of osteoporosis in men is beginning to bear fruit. As part of the Osteoporotic Fractures in Men (Mr. OS) study designed to identify predictors of non-spinal fractures in men, Dr. Eric Alwell and colleagues are trying to predict non-spinal fractures in men, and they have identified several factors that are reported in the *Journal of Bone and Mineral Research*. These factors include many of the same factors found in women (e.g., antidepressant use, history of fracture, falls in the last year, inability to complete a narrow walk trial, depressed mood, etc.). Mr. OS has been ongoing for about 8 years; the study represents followup efforts to the Study of Osteoporotic Fractures in Women, a 15+ year study funded by both the NIAMS and National Institute on Aging.
- In the NIAMS Intramural Program, Dr. Rafael Casellas and colleagues published a study in the *Journal of Experimental Medicine* addressing the question of why the immune system turns against parts of the body it is designed to protect, leading to autoimmune disease in some individuals. The researchers focused on B cells and showed that 10 percent of mature B cells in mice coexpress both light chains, and thereby, autoreactive B cells might escape a central tolerance because they have these two light chains on their surface; this phenomenon was not well known previous to this work.

### **Recent NIH/NIAMS Activities and Plans for the Future**

NIH Roadmap Version 1.5 efforts involve a series of programs jointly funded by the Institutes via the Common Fund and by the NIH Director that are intended to take money that was spent during the Roadmap Version 1 effort and continue to provide incubated space for new and important areas of research. In preparation for the transition of the first cohort of Roadmap initiatives out of the incubated space, the NIH began a process of soliciting ideas for the next set of Roadmap trans-NIH strategic initiatives for funding consideration in fiscal year 2008 (FY08). The criteria for the potential Roadmap 1.5 initiatives are the same as for Roadmap 1 (i.e., the proposed initiative must be truly transforming, have outcomes that synergistically advance the individual missions of the NIH Institutes and Centers (ICs) to benefit health, require participation from the NIH as a whole, and be something that no other entity is likely or able to do). Through the summer and fall of 2006, the NIH solicited ideas for initiatives. The following five areas were selected to be developed as major Roadmap 1.5 initiative proposals: (1) microbiome, (2) protein capture and proteome tools, (3) phenotyping services and tools, (4) inflammation as a common mechanism for disease, and (5) epigenetics. Other areas were designated for further development through small pilot studies, such as the genetic connectivity map and transient molecular motors. Coordination groups are being developed in the areas of regenerative medicine, pharmacogenetics, and bioinformatics. Furthermore, strategic planning groups are being put together in three other areas (i.e., training and centers, health disparities, and science of science administration). These plans will receive final review and priority recommendations in

the late spring of 2007 by the IC Directors before being submitted to NIH Director Dr. Elias Zerhouni.

With regard to the NIH Pathway to Independence Award (the K99/R00 award), the NIH has re-issued this Program Announcement for these awards given to highly promising postdoctoral scientists who are transitioning to becoming independent researchers. The NIAMS strongly supports this program and plans to fund four such awards in 2007 and 2008. There also is an NIH Directors New Innovator Award, which will support new investigators who propose highly innovative research projects with the potential of having an exceptional impact on biomedical and biobehavioral science. New investigators who have not yet obtained a traditional NIH R01 grant will be eligible; the proposed research may be in any scientific area relevant to the NIH mission. Dr. Katz noted that it is incumbent on the ICs to let their population of scientists know about these awards; 14-16 of the NIH Directors New Innovator Award will be made in 2007. The award includes \$300,000 in direct costs for 5 years, plus applicable indirect costs.

Dr. Katz also commented on the subject of women in biomedical careers. Dr. Zerhouni has created and is co-chairing a working group to examine the barriers facing women scientists; the details of these efforts will be posted on the NIH Office of Research on Women's Health (ORWH) Web site.

The NIAMS holds roundtable discussions every year. The purpose of these discussions is to help inform the Institute's scientific program administrators and Dr. Katz about the "hot" areas of science, what emphasis areas should be examined, and where the gaps are. Four roundtable meetings were held recently on: (1) musculoskeletal injury and trauma; (2) wound healing; (3) sex and gender factors in inflammation and immune-mediated diseases; and (4) rheumatoid arthritis, psoriasis, and psoriatic arthritis. Dr. Katz noted that efforts are made to include lay community participation in as many of these roundtable discussions as possible.

The NIAMS will be holding its annual Scientific Retreat this upcoming spring. Discussions will focus on epigenetics, inflammation, soft tissue imaging, and the Small Business Innovation Research/Small Business Technology Transfer Program.

In terms of information dissemination, the Institute has released a new 18-page NIAMS supplement, which was published in the summer 2006 issue of the *Journal for Minority Medical Students*, which exposes a large number of minority students and administrators to NIAMS program staff and research opportunities. The Institute also launched a CD-ROM in November 2006, titled "Lupus Information for You and Your Patients: Providing Essential Information to Health Professionals."

### **Budget Update**

In FY06, the NIAMS funded 247 new and competing continuation applications, for a success rate of 19.3 percent; the overall NIH success rate was 20.0 percent in FY06. Dr. Katz commented that this is as close to the NIH success rate as the NIAMS has ever come. A document providing detailed information on the distribution of the FY06 appropriation was given to Council members; Dr. Katz asked that Council members provide him with comments on

whether they would like this type of information for each fiscal year, and whether they feel that this information should be posted on the NIAMS Web site.

On February 15, 2007, the President signed into law a Joint Funding Resolution providing appropriations for FY07 (H.J. Res. 20/Public Law 110-5). The Resolution provides approximately \$620 million more for the NIH over FY06 levels. Although specific details were still being finalized as of this Council meeting, one item of note is a direct appropriation of funds to the NIH Office of the Director for the NIH Common Fund, which covers the Roadmap. In the past, Roadmap initiatives were supported by the NIH ICs. The funding level for the NIAMS in FY07 will remain essentially level with FY06, at \$507.8 million; however, the \$6.1 million originally earmarked for the Institute's Roadmap contribution will be available to the NIAMS for obligation. The NIAMS is proposing to make the entire \$6.1 million available for new and competing continuation research project grants (RPGs), as this is the Institute's highest priority. The additional funds will improve the estimated success rate in FY07 to an anticipated 17 percent.

To ensure the availability of an adequate pool of funds for new and competing continuation awards, the NIH will not provide inflationary adjustments for existing non-competing renewal awards in FY07, including modular grants and centers. Particular funding priority will be given to new investigators and first-time renewal applications from new investigators. Each Institute has been asked to fund a target number of new investigators equal to the average number funded over the previous 5 years. The goal for NIAMS in FY07 is 41. To reach this target, the Institute is in the process of developing a separate funding plan for new investigators.

The FY08 President's Budget request was released on February 5, 2007, at the same time as the Joint Funding Resolution. In addition to budget tables, the Congressional Justification document includes narrative sections about the Institute's programs and how funds will be allocated. Dr. Katz noted that even with the additional \$620 million to the NIH budget, the increase is not even with the inflationary increase; nevertheless, this increase is good news. Dr. Katz then introduced John Bartram, the NIH Associate Director for Budget, who provided additional details of the Joint Funding Resolution.

Mr. Bartram explained that the budgets for all NIH ICs are especially confusing this year. Normally, the current year budget passes before the next year's budget is submitted. This year, the NIH FY08 budget was submitted before the FY07 budget passed. He pointed out that the FY08 budget increases by about \$232 million, makes the assumption that the NIH is running on a continuing resolution, and does not take into account the additional \$620 million that NIH received in 2006. He further explained that the base that the FY07 budget was built on does not exist anymore.

The FY08 budget, viewed as a policy budget, increases by \$232 million; \$201 million of that is for the Global Fund to Fight HIV/AIDS, leaving approximately \$31 million for other NIH programs. In terms of a true NIH scientific research type of increase, the FY08 budget is about a \$32 million increase, which relative to other budgets that went out from the Federal Government, is not too bad—Mr. Bartram commented that budgets for most of the other Department of Health and Human Services (DHHS) components decreased.

In comparing the FY07 enacted budget (which is not the comparison point in the President's budget), Mr. Bartram explained that one would have to take the NIH increase and add it on top of the President's Budget (i.e., in order to create a baseline, that additional \$620 million would need to be added). However, neither of these scenarios takes any type of inflationary adjustment into consideration.

## **Discussion**

In response to a question from Council member Dr. Bevra Hahn, Professor in the Department of Medicine at the University of California, Los Angeles, School of Medicine, Dr. Katz explained that Congress and the President have identified a Common Fund, which is a new term for what NIH considers the Roadmap fund. The \$6.1 million that represented the NIAMS contribution to this fund in FY07 will now be covered by the Common Fund money that has been appropriated. As a consequence, the NIAMS now has that \$6.1 million and is planning to put it into the RPG line. Mr. Bartram added that in 2007, every Institute was going to put approximately 1.2 percent of their budget towards the Common Fund, for a total of about \$332 million from the ICs. In the enacted 2007 Appropriations Act, part of the \$620 million from Congress included that \$332 million to fully fund the Common Fund. As a result all of the ICs received an increase of 1.2 percent. This increase did not happen for other agencies. As a general rule, about half of the money at ICs goes to RPGs; about 52 percent in aggregate. Some ICs chose to put 100 percent of this 1.2 percent increase towards RPGs; most have elected to put at least 50 percent toward RPGs. Dr. Katz commented that Congress is expected to continue to appropriate to the Common Fund.

Dr. Josh Jacobs, an Orthopedic Surgeon at Rush University Medical Center and a member of the Council, asked if the proposed budget from the President will be about \$300 million less than the level at which the FY07 budget will actually be funded. Mr. Bartram replied that in pure dollar amounts, the enacted level of FY07 is roughly \$340 million above the President's FY08 budget. There is a \$232 million increase above the base that the FY08 budget was based on; that increase goes into different policy initiatives (e.g., the Global Fund to Fight HIV/AIDS). If Congress increased the NIH FY08 budget by \$340 million, some could argue that relative to the increase given to the Institute in FY07, it is still short by about \$220 million because of the programmatic adjustments. A more appropriate approach is to take the base increase from FY07 forward and add it on to the FY08 budget. Dr. Katz added that the FY08 budget is still in negotiation.

Dr. Susana Serrate-Sztejn, Director of the NIAMS Skin and Rheumatic Diseases Branch, noted that investigators often ask about the funding picture at NIH so that they can plan for their submission of applications in one fiscal year versus another. She asked for guidance in responding to these inquiries, given the President's FY08 budget. Mr. Bartram noted that he and his team, along with budget officers across the ICs, are working on determining the impact of the FY07 budget on FY08. The total number of new and competing grants in FY08 was expected to be one of the highest ever, about 10,188, and by placing the \$6.1 million increase into the RPGs, those competing grants in this year's cycle will go into non-competing grants next year. An operating plan for FY07 is being developed; once complete, the impacts of FY08's budget on the number of grants can be determined. Dr. Katz added that putting the \$6.1 million into the RPG

pool increases the Institute's non-competing pool for next year. The goal at the NIAMS and at the NIH is to keep things as consistent as possible.

Dr. Jacobs asked what this budget cycle's educational message should be for those organizations that go to the Hill and advocate for NIH funding. Mr. Bartram reminded the Council that as a federal employee, he is not allowed to lobby. He suggested that these organizations consider a message indicating that Congress's support in FY07 is greatly appreciated, and that this support aligns to many of the policy initiatives in the FY08 budget and in the FY07 fiscal policy, such as supporting first-time investigators, supporting vulnerable investigators, etc. It is hoped that this alignment of similar priorities will continue as the Hill examines the NIH FY08 budget.

Council member Dr. Cliff Rosen, Executive Director of the Maine Center for Osteoporosis Research and Education, asked for some insight into what happened in the FY07 budget that was different (apart from the continuing resolution issues). He asked whether any recent events might help in understanding what will happen in the future relative to Congress's intentions. Mr. Bartram commented that the Authorization Act helped to re-educate Congress on the value of NIH, and credit should be given to the many organizations that support NIH and help keep the Hill apprised of the value and importance of the NIH. These activities will be vital to continued success relative to funding from the Federal government. A combination of these organizations working together with a common message of the important value of science, first-time investigators, and first-time renewals has been critical. Dr. Katz applauded Mr. Bartram's efforts and his knowledge of the Office of Management and Budget and the Hill, as well as Dr. Zerhouni's perseverance, in their work to achieve as favorable a budget as possible for the NIH. He added that the National Aeronautics and Space Administration lost approximately \$570 million in this Joint Resolution.

In response to a question from Dr. Weinstein, Dr. Katz confirmed that a 17 percent success rate is anticipated for 2007 with the changes that have been implemented in terms of the budget. However, the success rate is directly tied to the number of submissions, and until that number is known, it is extremely difficult to determine what the bottom line will be.

#### V. UPDATE: INSTITUTIONAL CLINICAL AND TRANSLATIONAL SCIENCE AWARDS

Dr. Barbara Alving, Acting Director of the National Center for Research Resources (NCRR), reminded Council members that the Clinical and Translational Science Awards (CTSAs) grew out of efforts to re-engineer clinical research as part of NIH Roadmap efforts. The CTSA Program was created in part because of the recognition that implementing biomedical discoveries made in the last 10 years demands an evolution of clinical science. New prevention strategies and treatments must be developed, tested, and brought into medical practice more rapidly. Dr. Alving explained that CTSA awards will lower barriers between disciplines and encourage creative, innovative approaches to solving complex medical problems. CTSA awards will catalyze change by breaking silos, barriers, and conventions.

Dr. Alving explained that clinical research covers all studies of diseases and trials of treatments that take place in human subjects. Translational research describes the steps between a

fundamental discovery and its application in clinical medicine. She also explained that through the NIH Roadmap, CTSAs will create integrated environments for the clinical and translational researcher that can provide: (1) an academic home for clinical research; (2) support for protocol preparation, regulatory compliance, and data management; (3) support for participant recruitment and human subject safety monitoring; (4) education leading to advanced degrees in clinical research; and (5) specialized cores and services for translational research.

A total of 12 CTSAs were awarded in 2006; it is hoped that up to 60 are eventually funded at a cost of \$500 million per year. Currently, the NCCR is a \$1.1 billion Center, and it will have to undergo some significant changes and interact strongly with Roadmap programs to achieve this vision. These homes for clinical and translational science will interact robustly with industry and provide advantages and opportunities for grantees of the categorical Institutes such as NIAMS, and will have to demonstrate that other agencies are benefiting as well. Dr. Alving listed the first 12 CTSA awardees, noting that they and future awardees work as a consortium, adding to the strength and robustness of the program. Through this national CTSA Consortium, awardees will:

- Develop novel designs for clinical trials to ensure that patients with rare and common diseases benefit from new medical therapies.
- Produce enriched environments to educate and develop the next generation of clinical and translational researchers.
- Assemble interdisciplinary teams to cover the complete spectrum of research.
- Design new and improved clinical research informatics tools.
- Expand outreach efforts to minority and medically underserved communities.
- Enhance public trust and encourage participation in clinical and translational research.
- Forge new partnerships with private and public health care organizations.

Dr. Alving provided the Council with some examples of CTSA activities. Duke University has a project to translate bench-bedside findings to populations using advanced informatics and health services delivery methods. They are developing, in partnership with IBM, a Web-based system for patient records, so that patients can have their own personal health records. These health records may be a means for conducting clinical research in the future (e.g., to develop patient recruitment and participation in clinical trials). The University of California, San Francisco, is pursuing new opportunities with the San Francisco VA and Kaiser Permanente, and are hoping to create new community research centers to expand efforts in minority and medically underserved populations. Oregon Health Sciences University is developing informatics capabilities to partner with Kaiser Permanente NW Center for Health Research, Oregon Rural Practice Research Network, and Portland VA Medical Center for intervention research.

Informatics and outreach will be core features of the CTSA Program. The CTSA's will communicate with patients for clinical research and allow Principal Investigators (PIs) to communicate with patients at the end of research programs. Dr. Alving noted that a permanent, longitudinal record system could be very valuable for follow-up in this regard. Public trust can be enhanced through the CTSA's with the provision of participant and clinical interactions resources, a National Steering Committee of Regulatory Support, and increased trust between institutions and Institutional Review Boards. Dr. Alving explained that there will be a number of measurable results stemming from the CTSA Program. In the area of clinical research, the Program will provide for a reduction in the costs of conducting clinical trials, start-up time, overall duration, and duplication. The Program also will provide increased public awareness, trust, and participation in clinical research. Furthermore, enhanced access of clinical research data by researchers and regulatory organizations is envisioned.

The CTSA Consortium includes a PI Steering Committee (there are now 12 PIs from the 12 consortia, with plans to fully fund 8 new consortia this year). Subcommittees have been formed in the following areas: Biostatistics/Epidemiology/Research Design, Clinical Research Ethics, Clinical Research Informatics, Communications, Community Engagement, Education and Career Development, Evaluation, Participant and Clinical Interactions, Pediatrics, Public-Private Partnerships, and Translational (which facilitates advancements of novel translational research and technologies). Behind each CTSA subcommittee is an NIH committee working in partnership with the CTSA.

Dr. Alving noted that the CTSA faces difficulties in that they have many constituencies (e.g., NIH ICs, IC Directors, academic health centers, Congress). The CTSA Web site ([www.ctsa.org](http://www.ctsa.org)) includes each of the awardees' entire applications as well as background information on the CTSA. She also explained that there are numerous opportunities for interactions and collaborations with diverse communities. For example, CTSA's can develop partnerships with grantees in Institutional Development Enhancement Award (IDeA) States and at Research Centers in Minority Institutions (RCMIs). The IDeA states comprise 23 states and Puerto Rico that receive less than a certain amount of NIH funding because of their size, problems with populations, and distance. These developing states and their respective institutions offer geographically and ethnically diverse representation. IDeA and RCMI grantees have track records in training and mentoring.

In terms of the future, the CTSA's will stimulate an environment of change that will influence and include organizations involved in translational and clinical research as well as in health care delivery. The success of the CTSA Consortium will be measured in part by the degree to which it is inclusive; efforts are underway to develop partnerships in states and institutions that offer geographically and ethnically diverse representation. The ultimate goal is continuous improvements in the health of populations and individuals throughout the nation and internationally.

## **Discussion**

Dr. Katz opened the discussion session by commenting that the interaction and excitement that exist in the current CTSA's are tremendous. If that enthusiasm continues, the CTSA Program

will be very successful. Dr. Brian Kotzin, Vice President of Medical Sciences at Amgen, Inc., and a member of the Advisory Council, asked about the nature of the relationship between the CTSA's and industry. Dr. Alving responded that this type of relationship is emphasized, and there are many examples of creative partnerships. For example, at the Penn CTSA, there are many strong interactions with large pharmaceutical companies. There is a realization and recognition that to get new drugs out, whether for large numbers of people or for rarer populations, there is a need to interact closely with the biotechnology and pharmaceutical industries. The intent is to make these connections transparent and reduce barriers such as information technology issues. Dr. Katz added that in a general sense, there is an encouragement to leverage existing resources in all dimensions. The CTSA's are looking to leverage with industry, and industry should benefit from this interactive network as should all of academia and the public.

Council member Dr. Jack Parr, a consultant for Medical Technology Development, Inc., asked how and at what level industry becomes involved in the CTSA Program. He commented that a company probably wants to interact in a clinical or preclinical mode with a product or potential product. Dr. Katz explained that the NIH is not able to forge these types of relationships; they must be naturally occurring.

Council member Dr. Larry Raisz, Director of the University of Connecticut Center for Osteoporosis at the University of Connecticut Health Center, commented that in developing his group's planning event for the CTSA, the involvement of community hospitals has been a positive, and expressed the hope that more community hospitals become interested in and concerned about clinical research through this mechanism. Dr. Alving indicated that NIH Program Officers can be used to facilitate community involvement in CTSA's. Dr. Raisz asked if any Council members or NIAMS staff had any experience regarding contractual relationships with community hospitals, which is an area his group is struggling with. Dr. Alving noted that this issue could be brought to the attention of the CTSA's at a future meeting within the context of community outreach. One of the advantages of the CTSA Consortium is the development of standards or guidelines so that each interaction and agreement made does not have to be re-invented. Dr. Katz added that reaching out to community physicians might be an additional approach in terms of piloting projects such as a national clinical research associates program that is under consideration.

Dr. Hahn asked about the meaning of the terms "T1" and "T2." Dr. Alving explained that "T1" refers to "translational block 1," which goes from the laboratory and the basic investigator who has made a discovery and thinks it could turn into a drug, device, or clinical methodology and doesn't know how to take it there. The CTSA's provide that support; the investigator can go to the CTSA and connect with an expert who can provide guidance on next steps. The CTSA's also can facilitate courses, so that an individual who has a Ph.D. in Biochemistry could earn a Masters degree in Clinical and Translational Sciences. The term "T2" refers to "translational block 2," in which clinical results are moved into the community, making sure that the community understands them, and incorporating them into clinical practice.

## VI. LEGISLATIVE UPDATE

Mr. Marc Smolonsky, Director of Congressional Affairs and Legislative Policy at the NIH, discussed the NIH Reform Act. In 1944, the Public Health Service Act was passed, creating the NIH and the National Cancer Institute as a branch within the NIH. Since 1944, the NIH has grown tremendously, with 27 ICs today, most of which were created in statute. Until recently, Congress had been interested in increasing the size of the NIH, the scope of its authorities, and its budget—culminating in a doubling of the NIH budget between 1998 and 2003. Since 2003, the NIH has been undergoing a “post-doubling” period, during which the NIH has had flat budgets and been asked many questions from Congress about what has been done with the doubling in the budget, how the NIH has advanced research, how the NIH manages its programs, etc. This has been a challenging, yet predictable period for NIH, particularly at a time when there are so many budget cuts across the Federal government.

To further explain the context within which Congress began revisiting the Authorization Bill, Mr. Smolonsky explained that in recent years, Congress started looking at the Public Health Service Act, NIH’s existing authorities, and NIH’s current structure. A former NIH Director also looked at the structure and posited that the NIH should be reduced to six overall Institutes. In 2002, the Institute of Medicine (IOM) made similar observations, and also recommended establishing an escrow account (i.e., the current Common Fund). Congress went through more than 4 years of hearings, and Congressional staff interviewed virtually all IC Directors. While various draft proposals were being developed, Dr. Zerhouni suggested administratively creating a Common Fund as a set-aside. The NIH Roadmap was the prototype for this Common Fund, in which each IC set aside a certain amount of funds voluntarily for the Roadmap. OPASI was recently established to track many of these suggestions.

Mr. Smolonsky explained that the NIH Reform Act of 2006 was signed into law on January 15, 2007, by President Bush. The Act creates the Division of Program Coordination, Planning, and Strategic Initiatives, which incorporates the OPASI model. This Division is charged with identifying and reporting on research that represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between two or more ICs or would otherwise benefit from strategic coordination and planning. The initiatives that come out of this new Division will be funded by the Common Fund. Under this bill, the NIH Director has the authority to allocate money to this Common Fund, which would be distributed to the ICs in support of these initiatives determined by the new Division. Mr. Smolonsky noted that the law does not explicitly state what this Common Fund would look like (e.g., direct appropriation, set-aside, etc.); the appropriators have seized the initiative in the Joint Resolution for FY07, deciding to directly appropriate money into the Common Fund to support the Division of Program Coordination, Planning, and Strategic Initiatives projects. Based on the appropriators’ actions, the precedent of directly appropriating money into the Common Fund has now been set. The Authorization Bill, which is separate from the Appropriation Bill, indicates that the Common Fund will not be reduced below the previous year’s level, and when the Common Fund reaches 5 percent of the overall NIH budget, a review mechanism will be triggered to make recommendations on how to proceed. Mr. Smolonsky noted that the appropriators can always override these authorization requirements, however.

The Act also creates a Scientific Management Review Board for the NIH, which will be a standing review board that will assess the structure of the NIH at least every 7 years and make recommendations. This Board will be assessing, on an ongoing basis, how the NIH operates and will be reviewing the research portfolio of the NIH on a regular basis. Mr. Smolonsky stated that how this Board is set up, how it operates, and what kind of leadership it has will likely have a major impact on the future of the NIH.

The law also reaffirms or enhances the authority of the NIH Director to conduct program coordination across the ICs and reorganize the Office of the Director or the ICs themselves. These are not new authorities for the NIH Director, who through the Secretary of DHHS has always had the authority to conduct program coordination and reorganize the NIH even to the point of closing ICs (although this authority has not been used in the past). The bill requires a uniform coding system so that how the NIH funds research is transparent, uniform, and not duplicative in terms of budget numbers. The NIH has a knowledge management system that already has this project underway. The bill also eliminates many, if not all of NIH's reporting requirements and consolidates them into a biennial report. This will be a major departure from how the NIH currently provides reports to Congress and will affect all of the ICs.

In addition, the bill contains authorization levels for appropriations. Authorization bills authorize amounts to be spent, and unless the appropriators override those requirements, those amounts cannot be exceeded. The authorizers for 3 years running have significantly increased the budget of the NIH to \$30.3 billion in 2007, \$32.8 billion in 2008, and such sums as may be necessary beyond that. The authorizers, in essence, are indicating that the NIH has been underfunded, should get more money, and deserves more funding. Mr. Smolonsky noted that there probably is a connection between Congress speaking unanimously in the passage of this Act, and Congress then giving the NIH an increase in the Joint Resolution (this is particularly noteworthy given the treatment of other federal agencies related to their respective budgets). There also is a demonstration program in the bill that would coordinate research between the National Science Foundation, the Department of Energy, and the NIH on a modest scale. Mr. Smolonsky summarized his remarks by concluding that the NIH has emerged from a difficult period with an authorization bill that has laid the groundwork for increases in future appropriations.

## **Discussion**

Council member Dr. Martin Kushmerick, Professor in the Department of Radiology at the University of Washington, asked about the Scientific Management Review Board. Mr. Smolonsky explained that there is a legislative implementation plan in process—the ICs are part of an *Ad Hoc* Legislative Implementation Group that includes various subgroups looking at how to implement all of the provisions of the NIH Reform Act. These efforts are still a work in progress, and details regarding the Scientific Management Review Board have not been finalized. Dr. Katz noted that the implementation team should have a report available in the next 6-8 weeks. Mr. Smolonsky noted that Council members with questions about the details of the Act also can access information on the Office of Congressional Affairs and Legislative Policy's Web site.

## VII. MEMORANDUM OF UNDERSTANDING

Dr. Madeline Turkeltaub, Executive Secretary of the Council and Deputy Director of the NIAMS Extramural Program, explained that each January, a vote is required on a Memorandum of Understanding (MOU) between NIAMS staff and the Council. The MOU was distributed to Council members for review. The MOU indicates that following peer review, awards must be recommended for consideration of the Advisory Council. It specifies some specific concerns that should be brought to Council members' attention with regard to the applications that are presented to the Council. The action options that are available to Council members are listed in the MOU, which also contains further explanation of the process and procedure for *en bloc* concurrence for the applications. There are no changes to the MOU from last year. It is anticipated however, that language in the NIH Reform Act regarding Council action will be brought the Council as an addendum to the MOU.

A motion was made to approve the MOU. The motion was seconded, and passed.

## VIII. UPDATE ON CHANGES IN THE CENTER FOR SCIENTIFIC REVIEW

Dr. Tony Scarpa, Director of the Center for Scientific Review (CSR), opened his presentation by inviting Council members to contact him with any questions or suggestions they might have regarding the NIH peer review process. He noted that there are great challenges, but also great opportunities, to change a peer review system that has not been changed significantly in 60 years. Dr. Scarpa emphasized the great strategic national value of peer review for this country. He noted that the CSR currently receives 80,000 applications each year and reviews about 55,000 of them (the rest are reviewed by ICs according to programmatic needs). Last year, the CSR used 18,000 reviewers and held 1,800 study section meetings. The Center also employs 250 full-time Scientific Review Administrators (SRAs) and includes 220-230 different review groups, including some Special Emphasis Panels.

Why has U.S. biomedical research and biobehavioral research been so successful? The reason is not because this country spends more money in this area. Dr. Scarpa noted that the Federal Government of the United States spends less on biomedical research than most other countries (100% of NIH funds to universities and medical centers are awarded through peer review, compared with only 4-10% across Europe). In addition to creating the best science, peer review represents the "heart and soul" of the NIH. The NIH model for peer review has been admired and imitated elsewhere in this country and around the world. The peer review process also protects the NIH against outside influences.

Despite the success and value of the NIH peer review system, there are complaints. These include: (1) the process is too slow (it can take up to 3 years in some rare cases); (2) there are not enough senior experienced reviewers; (3) the process favors predictable research rather than high-impact, innovative research; (4) clinical research may not fare as well as other types of research; and (5) the time and effort needed to write, submit, resubmit, review, and re-review places a heavy burden on applicants and reviewers. Dr. Scarpa explained that part of the problem is that the diseases of America have changed; they are more chronic now and affect many organs, and the NIH as a whole is not necessarily well-suited to address diseases from this

perspective. Furthermore, the NIH has created a culture of independent investigators that has served this country well, but research today is done in large groups with collaborations between institutions.

Since Dr. Scarpa joined the CSR approximately 1.5 years ago, the Center has increased communication and transparency among its own staff and with the NIH. Uniformity and efficiency have been increased as well. At one point, the CSR was receiving the paper equivalent of 81.6 acres of forest during every cycle (i.e., every 4 months), and then shipping this large quantity of paper around the world. Now, electronic submission is being used. Electronic submission of applications has resulted in the removal of a layer of 170 processes and verifications from the time the grant comes in the door through the time the review is finished. Essentially, all aspects of the grant submittal-review process have been re-engineered in lieu of trying to incorporate electronic submission on top of existing processes and verifications.

Dr. Scarpa reported that the CSR has had incredible success in assigning grants to integrated review groups (IRG) or study sections directly by artificial intelligence, text fingerprinting, and multiple algorithm software. Essentially, submitted applications are compared with others in a database of more than 1,000,000 applications and sorted to the appropriate study section or IRG. By July 2007, all applications will be routed this way—a process that used to take 40 people and 40 days can now be done in less than half a day. Additionally, Dr. Scarpa pointed out that the CSR also now provides reviewers with non-refundable airline tickets instead of unrestricted tickets (the CSR is prepared to pay for one change to these tickets per reviewer per trip). This move alone is saving the CSR about \$12 million per year.

The Center also is making efforts to shorten the review cycle, with the goal of providing applicants with their reviews and scores within 3 months from the date of submission. This will allow the CSR to conduct three review cycles per year instead of just one. Currently, the CSR posts all summary statements within 1 month following the study section meeting, and new investigator summary statements are posted within 1 week. The CSR began a pilot program that would allow some new investigators to submit immediately, so that they would receive their revisions early on and would have a month or more to reply. This pilot has been extremely successful, and those who submitted early fared two times better than comparable applicants who did not submit early. In view of that, the CSR has increased the number of new investigators who are eligible to submit early to 3,000. By June 2007, this number will reach 5,000; Dr. Scarpa noted that by November 2007, all of the new investigators (25% of the total number of applicants) will have the opportunity to submit early and have up to three review cycles per year if they wish.

The CSR often hears complaints from applicants who feel that the study section reviewing their application was not suitable. About 7 years ago, there was a realignment of the study sections, with mixed results. The CSR has received enough complaints along these lines that it has decided to review every IRG (each IRG contains about 5-7 study sections). The Center, through six open-house workshops, also is appealing to the scientific community at large to ask for advice on whether science is sufficiently reviewed in study sections. Participants will be asked for their input on issues such as whether the science is appropriately evaluated, whether the CSR

should be doing something differently, what major issues in each discipline will be arising, and what the CSR can do to prepare for them. These workshops will be held every 2 months. Dr. Scarpa commented that peer review will only be as good and effective as the reviewers. The CSR is doing more to recruit and retain more high-quality reviewers and decrease the burden on applicants and reviewers. Five years ago, the CSR received 46,000 applications; today the Center receives 80,000 per year. In terms of R01 and R21 applications, the number has doubled from 5 years ago to about 42,000 this year. The primary reason for this is that during the doubling period at the NIH, about 15,000 new investigators started, and they continue to write grant applications. Overall, investigators are writing and submitting more applications, too. In the past 30 years, the number of grants written per applicant was about 1.2. However, this has increased today to a rate of 1.4 or 1.5 per applicant. In addition, the average load for the reviewers was about 11 applications per reviewer. Today, each reviewer is responsible for about 6 applications; the number of applications has almost doubled and the reviewers' loads have been cut in half.

The CSR also is trying to establish additional review platforms. For example, the Center has started electronic reviews that include telephone-enhanced discussions, video-enhanced discussions, and asynchronous discussions (Web chat). More than 2,000 study sections have been conducted via Web chat. Electronic reviews entail the same process for the reviewers, but without the travel and face-to-face interaction. Dr. Scarpa noted that physicists and computational biologists in particular have responded very favorably to holding study sections through asynchronous discussions. The CSR has a goal of carrying out 10 percent of reviews electronically in 2007.

Another near-term solution for recruiting and retaining the best reviewers is to shorten the application length. The advantages of shorter applications include the fact that each reviewer can review more applications, study sections can be smaller, and more experienced reviewers can be recruited. Also, the reviews can be more focused on impact and innovation and less so on approach and preliminary results. An inter-NIH committee has been considering shortening the R01 applications, with strong support from IC Advisory Councils and Directors, scientific leadership, etc. A Request for Information found that 74 percent of more than 5,000 scientists indicated that they are in favor of having shorter applications. Additional possibilities being considered by the CSR include abolishing all deadlines and having a rolling review system, utilizing editorial board reviews, and providing reviewer rewards. In addition, the Center is exploring the possibilities of recruiting reviewers from outside the United States.

Dr. Scarpa noted that the peer review system is an integral part of the NIH that has served the ICs incredibly well. The 250 SRAs working at CSR are the unsung heroes of the peer review system. He concluded his remarks by noting that the application of results from peer reviewed research prevented approximately 815,000 deaths in 2000. The true value of peer review is in the life of millions of Americans who are alive, cured, or in remission because the peer review system identified the best research and the best cure for their diseases. Dr. Scarpa also noted that the results of peer reviewed research extend beyond the United States and provide value to the entire world.

## Discussion

Dr. Katz noted that an August 14, 2007, CSR Open House Meeting will include leaders from various professional societies as well as leaders of lay organizations that have a stake in the peer review process. Council member Dr. Jouni Uitto, Professor and Chair, Department of Dermatology and Cutaneous Biology at Jefferson Medical College, emphasized the need to move away from reviews that include too many assistant professor-level reviewers who often are too concentrated on the fine details of applications. It is critical for the CSR to do whatever it can to retain senior reviewers. In terms of recruiting reviewers from overseas, Dr. Uitto cautioned that many international organizations have a completely different approach to evaluating science and grant applications. A rigorous educational program will be needed to train these potential reviewers from other countries. Dr. Uitto also noted that he would be in favor of shortening the length of applications. Dr. Scarpa responded that the Fogarty International Center is required to recruit a certain number of foreign reviewers, and that the NIH awards a fair number of grants abroad, so it makes sense to recruit reviewers from foreign countries. In terms of the experience of reviewers, Dr. Scarpa noted that the CSR has reduced the number of assistant professors by half, although there is a point at which these individuals are needed because no one else is available. Reducing the overall number of reviewers required should help in this regard.

Dr. Diamond agreed that the most important work done in the scientific community is identified through the peer review process. She noted that reviewers are not necessarily trained to serve as reviewers, and their performance as reviewers is not evaluated. A culture of criticism, as opposed to a culture of advocacy, seems to have evolved. With the opportunity to shorten grant applications, it may be possible to also educate reviewers and implement some type of ongoing evaluation. She added that reviewers who always score applications low need to understand that they are hurting the applications that they like. This is too important of a job to not pay attention to how they perform. Dr. Scarpa noted that in his experience, it is infrequent that a reviewer will consistently score applications too low. Generally, the opposite occurs in the sense that study sections generally score applications high, and it is not necessarily bad when there is not consensus on an application. Dr. Diamond also noted that during the years of NIH budget doubling, the notion of “three strikes and you’re out” was introduced. That made good sense at the time, because funding was generous. In the current climate, applications in the 15<sup>th</sup> percentile are not funded sometimes, even though study sections may think these applications have been funded.

Dr. Diamond expressed concern that some of the applications that reviewers like most are falling off the radar screen. Dr. Scarpa took the opposite view, noting that an application that barely misses the funding range does not need to be fixed. The IC should be able to pay for it if it sees fit—waiting 9 months and being reviewed again will not lead to improvements in the science. Dr. Katz noted that an alternative approach may be to only allow one revision to an application. Dr. Diamond noted that by not setting a limit on the number of reviews, it requires the reviewers to indicate to applicants who wrote poor applications that the CSR does not want to waste their time or the researchers’ to review them again.

Dr. Rosen, who served as Chair of a study section during the NIH budget doubling period, applauded the recommendations presented by Dr. Scarpa. He noted that SRAs have commented to him that the reviewers they wanted to promote to permanent positions on study sections were being held up in a review process pending their permanent appointment. Dr. Scarpa acknowledged that becoming a permanent study section member is a lengthy process, mostly attributable to Federal Advisory Committee rules. Dr. Rosen mentioned that a review of the study section reviewers would help to maintain enthusiasm and interest while this process was underway. Dr. Scarpa agreed, noting that he would like to implement such a system, but it is unclear what criteria would be used in such an evaluation. Dr. Rosen suggested that the SRA and Chair of the study section could work together in an evaluation effort.

Dr. Kathleen Green expressed concern about missing some of the around-the-table benefits associated with face-to-face review meetings. The apprenticeship aspect of being a reviewer is critical, and junior people are going to have to be brought into the fold gradually—and being around the table is the best way to season these younger reviewers. Dr. Scarpa noted that the CSR does some training activities through mock study sections, but these are very time intensive. He also noted that any rumors circulating about the CSR trying to replace face-to-face review meetings completely are false. Dr. Green also asked about the Request for Information results on shortening the length of applications. Dr. Scarpa indicated that one-fourth of the respondents wanted to maintain the current page length or make it longer; about 50 percent pushed for a 15-page length, 20 percent wanted a 10-page length, and 3-5 percent advocated for fewer than 10 pages. Dr. Katz added that if the length of the application is shortened, there has to be some education of the reviewers so that they review and score appropriately.

Dr. Weinstein noted that he serves as an editor for the journal *Spine*, and commented that the editorial board approach is an interesting one. They provide feedback to reviewers on their reviews so that they are graded on every review. Training sessions are available for reviewers who need help honing their review skills.

Dr. Kushmerick noted that all of the points discussed by Dr. Scarpa and Council members will require a change in overall culture. The scientific community knows that the current funding level is less than attractive. He commented that it seems that a reviewer is put in the position of picking the one application he or she likes most and try to sell it, while letting the other ones go. Dr. Scarpa agreed that a culture change would be needed for many of the changes being considered at the CSR. For example, if applications were cut from 25 pages to 12 pages, applicants would have to write differently and reviewers would have to evaluate differently.

Dr. Jacobs asked if the CTSA mechanism could serve as a vehicle to help with some of the training and recruiting aspects being considered by the CSR. In 5 years, there will be 60 institutions with CTSA awards, and part of the training component for both new and established investigators can be grant review. The CTSA's will include both clinical and basic researchers, so it may be possible to leverage this CTSA mechanism. Dr. Scarpa commented that this is an excellent idea.

Dr. Kotzin congratulated Dr. Scarpa on CSR's efforts to improve the peer review process. He touched on the issue of risk and novelty being embraced by study section members and

expressed concern that there may have been some movement in the opposite direction given current funding levels. Dr. Scarpa commented that the NIH, with a \$24 billion budget, should have a process that allows for deep innovation. He also expressed concern that the Federal government and universities may not know how to handle deep innovation, adding that everything funded by the NIH should be of high impact and significance. In response to a question from Dr. Parr, Dr. Scarpa responded that the CSR has a standard guideline and instructions for review of each of the type of grants being reviewed by the Center.

#### IX. ORGANIZATION AND STRUCTURE OF THE NIAMS EXTRAMURAL SCIENCE PROGRAMS

Dr. Katz explained that, as is consistent with Institute practices over the last 12 years, the NIAMS has reviewed various aspects from time to time, and about 15 months ago began an assessment of the Extramural Program. Dr. Joan McGowan, Director of the NIAMS Musculoskeletal Diseases Branch, explained that the review was led by an external review committee that included three experienced NIH administrators (one from the CSR, one from the National Institute of Neurological Disorders and Stroke, and one from the National Eye Institute). An additional six external review members who were former/current Council members also participated, as did three internal NIAMS staff members. The review panel was charged with recommending an organizational structure for the Extramural Program that would most effectively: (1) achieve the NIAMS mission, (2) facilitate the personal and professional development of staff, and (3) meet the needs of the scientific communities whose research the NIAMS Extramural Program supports. The following issues and opportunities were identified as a result of the review:

- The scientific and management complexity has grown without any change in the extramural structure.
- The NIAMS has seen an increase in the number of grants as well as the NIH cross-cutting activities without a commensurate growth in staffing.
- Scientific alignments of the programs could be re-examined to enhance synergy, determine areas of new growth, and identify opportunities for new and existing scientific staff.

Dr. McGowan explained that Dr. Katz has given the NIAMS a somewhat simplified structure that separates the two scientific areas of musculoskeletal diseases and skin and rheumatic diseases from the area of extramural research activities (e.g., grants, the scientific review process, management of the Council, and coordination of NIAMS as a whole).

Dr. Turkeltaub explained that the vision of the NIAMS Extramural Programs is one that is built on a foundation of exceptional people and processes so that the Institute can provide better services to the community. The vision for the Extramural Programs includes providing a work environment that allows staff to grow, attracting and retaining talented individuals, and including processes and procedures that will be seen as best practice while meeting the needs of the NIH and the communities that the NIAMS serves. The NIAMS intends to maximize the potential of the Institute within the NIH and the potential of the Institute's communities, providing them with

the information they need to be competitive in the grants environment. Efforts also are underway to implement the NIAMS mission in the best way possible through the Extramural Program.

Dr. Turkeltaub described the goals of the NIAMS Extramural Program Leadership Team as follows: (1) develop creative approaches to advancing the NIAMS mission through extramural research leadership and support; (2) operationalize the Extramural Reorganization Plan; and (3) develop an efficient, interactive, collaborative work environment that encourages scientific excitement and administrative discipline that better meet the needs of the NIAMS, NIH, and the communities that the Institute serves. Dr. Turkeltaub commented that the Roadmap opportunities at NIH that encourage communication across and among multidisciplinary and interdisciplinary groups is occurring through the NIAMS Extramural Programs.

The NIAMS Extramural Program includes extramural research activities, which includes the Scientific Review Branch, the Grants Management Branch, clinical research project management, management support (e.g., the Division of Extramural Activities Support, oversight of contract services), and support for the ORWH. This component of the Extramural Program also serves as the Secretariat for the Council.

The NIAMS Extramural Program's Skin and Rheumatic Diseases Branch encompasses keratinocyte biology and diseases, inflammatory and autoimmune diseases of the skin, extracellular matrix biology and diseases, innate immunity, cellular immunity, genetics, clinical trials and health services research, and biopsychosocial research. The NIAMS Extramural Program's musculoskeletal diseases area includes bone biology; bone diseases; muscle development and physiology; muscle disorders and therapy; cartilage and connective tissue; orthopaedics; the Osteoarthritis Initiative (OAI) and diagnostic imaging; and musculoskeletal development, tissue engineering, and regenerative medicine. In terms of cross-cutting issues, Dr. Turkeltaub listed the following identified priority areas: genetics, Clinical Trials Working Group, regenerative medicine, behavioral issues, and biomarkers.

Dr. Serrate-Sztejn noted that one of the comments and criticisms that came from the external review was the way that the NIAMS portfolios were designed and administered was not in keeping with recent advances in science. In response, the NIAMS has completed a portfolio analysis and design that identified many of the research issues and areas described by Dr. Turkeltaub. The Institute also implemented a new program in research translation (the Centers of Research Translation), developed a new bone partnership, leveraged existing investments (e.g., the Genetic Association Information Network), and improved clinical coordination. At the NIH level, the NIAMS has taken the lead on a number of initiatives, including the patient-reported outcomes measurement information system—or PROMIS—network and the OAI. Dr. Serrate-Sztejn also described some recent NIAMS accomplishments in terms of administration. For example, the Institute has fully staffed the Extramural Program as recommended in the Reorganization Plan. The Institute is developing a shared management model, and an Extramural Staff Retreat was held which focused on the establishment of cross-cutting groups and the development of Standard Operating Procedures to enhance program management. She closed the presentation by describing the following plans for the NIAMS Extramural Program:

- Realign the scientific programs according to evolving science models.
- Emphasize the development of collaborative approaches through effective teamwork.
- Explore opportunities for emerging areas.
- Enhance collaborations, interactions, and sharing through participatory leadership.
- Develop a more aggressive approach to partnerships.
- Incorporate creative approaches to funding.
- Modernize operating procedures.
- Review funding mechanisms.

## **Discussion**

Dr. Kushmerick commented that the review appears to be more focused on administrative structure and support. He asked whether there was a mechanism by which scientific areas of focus and progress in the grant portfolio can be communicated to other investigators. Research progresses by chance connections in many instances and investigators are limited to conversations at meetings and the literature to find out what is currently going on in other laboratories. Is this a good idea? It might be, if handled correctly, and it might lead to faster progress in some areas. Dr. Kushmerick noted that NIAMS portfolio managers might be in the best position to do this. Dr. Katz explained that NIAMS tries to communicate advances, when they can be communicated, through its Office of Communication and Public Liaison in a proactive way. Even incremental advances are put out to the community in various ways, such as press releases and fact sheets. Dr. Katz acknowledged that on a regular basis, there is a tension related to the confidential information of an investigator. Dr. Serrate-Sztein added that as the NIH moves to keep all records electronically, there have been preliminary discussions for changing how progress reports from funded investigators are put together—these changes may include publicly available statements.

Dr. McGowan noted that one of the goals is to emphasize synergies, and the Institute is actively working to identify these synergies without revealing any proprietary information. This effort is important for helping to achieve team-based science and avoid duplicative efforts. Dr. Katz added that NIAMS Program Directors can provide assistance in this regard, drawing on their knowledge of what is in the portfolio. The Program Directors are here to help the scientific community, and the community should utilize this assistance. Dr. Weinstein noted that releasing information or misinformation often can be damaging to some investigators. Dr. Kushmerick agreed that it would not be in anyone's best interest to release information that is preliminary or proprietary.

Dr. Jacobs, who participated in the external review, reported that there was a fair amount of discussion on the position of the Director of the NIAMS Extramural Program. He asked if there was a shared model with three individuals co-directing the Extramural Program. Dr. Katz added that the individuals have different areas of responsibility. Dr. McGowan explained that the model, as it was described, incorporates all responsibilities and authority previously vested in the role of the Director of the Extramural Program. Two scientific areas have been divided out, because the science is so complex and interactive; it was felt that for one person to be responsible for all of the science and the administrative and coordination activities would be overly burdensome. Drs. McGowan, Turkeltaub, and Serrate-Sztejn serve on an executive group with the two Intramural Research Program Directors and Dr. Katz, and it is more likely that Extramural Program leadership can manage the breadth of the science and administrative/coordination activities in this model.

Dr. Jacobs asked about the role of the NIAMS Deputy Director, and how that position interfaces with this new model for the Extramural Program. Dr. Katz explained that the new Deputy Director, when identified and hired, hopefully will bring scientific excellence to the Institute, and will have shared responsibilities with the Director in many areas. The Deputy Director will provide another dimension of science beyond the Director's expertise and will be an individual capable of leading the Institute in Dr. Katz's absence while providing value added to the NIAMS.

Dr. Hahn asked whether there was a model for screening grants that are going to be reviewed that allows for communication to the PI, prompting PIs to check the NIH Web site in a way that potentially could be useful in turning them on to available resources and current work. Dr. Katz emphasized that the Institute is trying very hard to find ways to best communicate available resources and information. Very often, leadership at various professional organizations does not know the full extent of what is available. There are vast resources in terms of genetics, animal models, etc., that are available. Professional organizations, through their communications such as Web sites and newsletters, are helping to alleviate the problem. Dr. Hahn suggested that links to appropriate resources could be included in the instructions for preparing and submitting a grant application. Dr. Katz noted that the NIAMS has done this in the past in calls for proposals. This type of communication also is important in terms of preventing applicants from submitting proposals for work that already has been done or is being done.

Dr. McGowan noted that the National Center for Complimentary and Alternative Medicine (NCCAM) has very limited funds and cannot redundantly pursue all of the different complimentary and alternative medicine approaches. They have put a hold on applications in a certain area because they already have ongoing work in this area, and the NCCAM wants to see outcomes of this work before funding similar investigations. The NIAMS potentially could adapt this approach, but only in a few very specific areas. The Institute has to be very proactive in terms of the expensive clinical applications. Dr. Katz added that any project costing more than \$500,000 needs permission for researchers to apply.

## X. NIAMS SPECIAL POPULATIONS REPORT

Dr. Turkeltaub presented the *Biennial Report on NIAMS Progress in Monitoring Women and Minority Issues in Grant Applications: FY 2006* to the Council. She provided a historical perspective on the issue of inclusion of women and minorities in clinical research, explaining that in 1986, there was an NIH policy urging the inclusion of women in clinical research. This policy was followed in 1987 by a similar policy encouraging the inclusion of minorities. The 1993 NIH Revitalization Act mandated that women and minorities must be included in all NIH clinical research studies (the Act was implemented in 1994). In 1998, the NIH also implemented an inclusion of children policy. Since 1998, the NIH has released periodic updates to these rules. In 2000, the NIH implemented a new clinical tracking system so that target populations in all clinical trials could be tracked closely. In 2001, inclusion compliance was included in priority scoring, and the population categories were modified to correspond to the U.S. Census.

Dr. Turkeltaub described the Council's role related to clinical tracking. Aggregated IC data are reviewed every other year by the Council, which then approves/amends a report to the ORWH for submission to Congress. With regard to the NIAMS portfolio for FY06, there are 1,240 total funded research grants, including 134 human subjects studies with enrollment data in the tracking system. Seventy-five of these protocols have zero enrollment (i.e., the data have not yet been submitted, enrollment has not yet begun, the data may be duplicate data from other studies claiming that population, they may be small populations with less than 10 individuals). In examining enrollment by sex, of a total of 78,435 participants enrolled in NIAMS studies, 42,248 (53.9%) are female. This level is consistent with the NIH overall. Minority enrollment is at 18,403 (23.5%) individuals. Dr. Turkeltaub broke down the enrollment rates for various minority groups (African Americans represent 13 percent of total enrollment, Asians represent 5 percent, Hispanics 4 percent, etc.). These numbers are in line with the other NIH ICs, although the NIH aggregate data do show a slightly higher percentage (which relates to four very large NIH grants in Africa in which all of the participants are listed as African Americans).

A motion to approve the report was made, seconded, and approved with two abstentions.

### **Discussion**

Dr. Kotzin asked about the number of women enrolled in NIAMS studies, noting that many of the studies in the NIAMS portfolio might be predominantly female-related (e.g., large studies of post-menopausal women). He asked whether other grants that should not have a gender bias have equal representation of males and females. Dr. Katz explained that NIAMS tracks all of the studies, and there are other studies in the NIAMS portfolio that skew in the other direction, toward males (e.g., the Mr. OS Study). Dr. Turkeltaub added that the NIAMS has a large grant studying men in Hong Kong who have osteoporosis.

Dr. Diamond asked about pediatric data. Dr. Turkeltaub explained that pediatric data are examined in priority scoring, but not tracked. Dr. Hahn noted that Council members were not presented with any data on the percentages of women and minorities included in clinical trials across the NIH overall, making it difficult to put this report in context. Dr. Katz added that aggregate NIH data will be sent out to Council members in light of these discussions. Dr. Kotzin

noted that having the data presented in this manner makes it difficult to determine whether the NIAMS is achieving its goals related to minority and women enrollment in clinical trials. Dr. Katz emphasized that the goal is reached in many ways, one of which is via the application process and the adherence to inclusion of children, women, and minorities in research projects. If they are not included in the research plan, there is a hold placed on the application. He asked the Council if it would be helpful to provide enrollment data from each of the 134 studies. Dr. Kotzin commented that it might be helpful if there was a way to organize the 134 studies to determine whether they are meeting their respective enrollment goals.

Dr. Serrate-Sztein explained that each investigator sets targets in terms of enrollment of minorities, women, and children at the beginning of their award. The Institute collects that information, and on an annual basis compares what the researchers report versus what they indicated they would recruit. When there is a large discrepancy, the NIAMS requests additional information on how the investigators plan to address it. She explained that for the most part, there is no provision in the NIH to suspend a study because a particular group is not meeting the enrollment numbers it agreed to meet. Dr. Katz commented that when enrollment targets have not been met, IC Directors historically have, on occasion, met directly with the investigators to insist that actions were taken to meet enrollment goals.

Dr. Diamond suggested that it would be useful for Council members to know what the target was, what was approved, what investigators wanted to be looking at, and what actually was examined for the studies in the NIAMS portfolio. These data would address in this report what the Institute is obligated to generate, and it might become more apparent if there are particular populations that no one is able to recruit and things that need to be looked at more in a systematic way.

#### XI. MUSCULOSKELETAL DEVELOPMENT, TISSUE ENGINEERING, AND REGENERATIVE MEDICINE PROGRAM PORTFOLIO

A discussion of the Musculoskeletal Development, Tissue Engineering, and Regenerative Medicine Program portfolio took place during closed session.

#### XII. REPORT OF THE BOARD OF SCIENTIFIC ADVISORS

A report from the Board of Scientific Advisors was presented during closed session.

#### XIII. CONSIDERATION OF APPLICATIONS

The Council reviewed a total of 588 applications in closed session requesting \$139,586,428 and recommended for \$139,586,428.

#### XIV. ADJOURNMENT

The 61<sup>st</sup> National Arthritis and Musculoskeletal and Skin Diseases Advisory Council Meeting was adjourned at 4:00 p.m. Proceedings of the public portion of this meeting are recorded in this summary.

I hereby certify that, to the best of my knowledge, the foregoing summary is accurate and complete.

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Madeline Turkeltaub, C.R.N.P., Ph.D.  
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and Musculoskeletal and Skin Diseases  
Advisory Council

Deputy Director, Extramural Program  
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